28. (New) A sample solution treating instrument comprising:

(a) a sample introducing part;

(b) a control means for converting a sample solution to a condition for analysis by a biosensor that electrochemically measures a specific component in the sample solution; and

(c) a sample releasing part;

wherein the instrument is adapted for use with a biosensor that electrochemically measures a specific component in a sample solution, but the instrument is not physically coupled to the biosensor, and wherein the control means comprises a control means agent selected from the group consisting of a catalyst which is capable of converting an interfering substance in the sample solution to a harmless substance having no adverse effect on a measurement result of the specific component obtained by analysis with the biosensor, an adsorbent which is capable of adsorbing and removing an interfering substance from the sample solution, and a buffer agent, which is capable of adjusting a pH of the sample solution to a pH range adequate for an activity of an enzyme in the biosensor.

REMARKS

Claims 19-28 are pending in this application. Claims 11-18 have been cancelled without prejudice. New claims 19 to 28 do not incorporate new matter. Support for the new claims is found at least in claims 1-7 and Figures 1-5 as initially filed. Further, support for the language in the new claims related to the means by which the biosensor analyzes the special component is found at least in the specification at pages 1-6.

Each of the rejections set forth by the Examiner is addressed in turn below.

I. Rejection Under 35 U.S.C. § 112, Second Paragraph.

At page 2 of Paper No. 11, the Examiner has rejected claims 11-18 under 35 U.S.C. § 112, second paragraph, as being indefinite. In particular, with regard to claims 11 and 18, the Examiner indicates that the recitation of the control means being separate from the biosensor renders the claims vague and indefinite. Claims 11 and 18 have been cancelled, and the new claims specify that the control means is physically separate from the biosensor. Support for this claim language is found at least in Figures 1-5, as filed.

The Examiner also indicates that he believes use of the phrase "the measurement results" to render claim 12 indefinite. Claim 12 has been cancelled. The new claims 19-28 do not contain this language, but instead recite that the interfering substances have no adverse effect on a measurement result of the specific component as analyzed by the specified biosensor.

In view of the foregoing, it is submitted that the Examiner's § 112 rejections are no longer applicable; therefore it is respectfully requested that the Examiner reconsider and withdraw these rejections.

II. Rejections Under 35 U.S.C. § 102.

At pages 3-5 of Paper No. 11, the Examiner has rejected claims 11-18 under 35 U.S.C. § 102(b) based upon one or more of the following references, each taken individually:

A. U.S. Patent No. 5,271,819 of Bockowski ("Bockowski");

B. U.S. Patent No. 5,378,635 of Yasuda *et al.* ("Yasuda");

C. U.S. Patent No. 5,079,170 of Rosman *et al.* ("Rosman");

D. U.S. Patent No. 4,270,923 of Kondo *et al.* ("Kondo");

E. U.S. Patent No. 4,654,311 of Khanna *et al.* ("Khanna");

F. U.S. Patent No. 5,492,834 of Liu *et al.* ("Liu");

G. U.S. Patent No. 4,279,618 of Barden *et al.* ("Barden"); and

H. U.S. Patent No. 5,945,345 of Blatt *et al.* ("Blatt").

The applicants have cancelled claims 11-18, but traverse this rejection, should it be applied to any of new claims 19-28, for the reasons set forth below.

The Invention

The invention of this application is a sample solution treating instrument that allows for the simple adjustment of the selected sample solution containing a targeted specific component, such as saki moromi, or a nutritional drink, in order to place it in a condition suitable for a more rapid and more accurate analysis by a physically separate biosensor. The biosensor then accomplishes quantitative measurement of a specific component in the sample solution, by electrochemical means, for example, by detection of an oxidation current. Prior to this analysis, the sample solution is treated in the control means of the sample solution treating instrument, which is itself equipped to place the sample solution in a proper condition for analysis by the biosensor by use of a control means agent such as various buffer agents, adsorbents, and/or catalysts.

For example, the control means may contain catalysts capable of converting interfering substances, such as vitamin B_2, vitamin C, tannic acid, or anthocyanin, into "harmless" substances that the biosensor is less likely to erroneously detect as an analyte, thereby avoiding false positives. The control means may also contain an adsorbent material that may function to adsorb and remove any interfering substances, or it may contain a buffering agent, which serves to adjust the pH to a level at which the enzyme(s) contained in the biosensor may function efficiently.

As is described in the Background section of the specification and in some of the prior art of record, conventional practice for detection of an analyte by electrochemical measurement, for example, by measurement of an oxidation current, may utilize a biosensor having a component integral to, or in close proximity with, the biosensor electrode, which contains an additional means intended to act to remove or neutralize any interfering substances, in order to place the solution in a better condition for the detection reaction of oxidation current. This additional means does not function in the detection reaction, which is the primary activity of the biosensor, but is complementary to such activity. Detection processes using a biosensor configured in this manner suffer from several drawbacks. For example, because the biosensor and the additional means are exposed to the sample solution almost simultaneously, the conditioning of the sample solution is not necessarily completed before the analyte detection reaction is accomplished. Thus, the measurement obtained may be substantially affected by interfering substances, in spite of the presence of the additional means. Additionally, use of biosensors containing a conditioning means integral to or in close proximity with the biosensor electrode does not permit use of the same biosensor with different sample solutions, if such solutions contain disparate interfering substances having differing chemical behaviors, and which therefore may not necessarily be efficiently eliminated or reduced in the same manner or by the same processes.

The § 102(b) Rejections

The Examiner has maintained his anticipation rejections based upon two of the previously cited prior art references (Bockowski and Barden), and has further cited six more prior art references, asserting that each individually anticipates one or more claims of the present invention.

Bockowski discloses a sensor electrode physically coupled to one or more filters, made of materials such as polymers, and adsorbents such as activated carbon. The sensor electrode and the filters are located within close proximity to one another, and are physically coupled in an electrode support housing. *See, e.g.,* Figures 1 and 2 of Bockowski.

Yasuda discloses a method of detecting catecholamines, such as dopamines, norepinephrine, and epinephrine by using fluorescent labeling. The detection method involves the steps of (1) obtaining a biological sample and adding, *inter alia*, maleimide to the sample prior to adding a fluoroescence inducing reagent; (2) subsequently adding a fluorescence inducing reagent to the biological sample to obtain a "fluorescence inductor" (*i.e.*, a solution containing catecholamines with an activated fluorophore); (3) supplying the fluorescence inductor to a microsyringe from which it is injected into a high speed liquid chromotography device; and (4) detecting the fluorescence intensity of the fluorescing catecholamines using a fluorometer. *See, e.g.,* Fig. 1. Yasuda does not disclose a means capable of converting interfering substances for analysis by a physically separate

biosensor which quantifies a special component by detection of an oxidation current. The device disclosed by Yasuda for accomplishment of the method is a microsyringe (into which the sample solution, containing both maleimide and fluorescence inductor is introduced) that is coupled via tubing to a series of separation columns and to the fluorometer, where the detection is accomplished.

Rosman discloses a sample applicator for use in performing immunoassays. The sample applicator is used to transfer liquid during immunoassay preparatory procedures. The applicator of Rosman contains a filter capable of removing particulate matter or adding reagents to the liquid sample. The liquid sample is expelled from the Rosman applicator, then utilized in an immunoassay to allow for detection or quantification of the target protein.

Kondo discloses a method of removing interfering components and elements of turbidity present in a fluid for use in an immunologic pregnancy test by contacting the biological fluid with a carboxylic acid-type cation exchange resin fiber filter. Kondo teaches that the filter resin is packed into an open-ended tube through which the fluid is passed. The amount of human chorionic gonadotropin in the filtered biological fluid is determined by a subsequent immunologic assay.

Khanna teaches a method of preparing a serum sample in order to enhance the accuracy of measurement of digoxin in an assay. The Khanna method requires contacting a serum sample with a chromatographic column containing alkylated silica gel, washing the column, and eluting the digoxin from the chromatographic column. The purified digoxin is then assayed using labelling and/or immunologic means such as enzyme labels, fluorescence assays, or radioimmunoassays.

Liu discloses a means of preparing a body fluid composition for urine protein analysis. The process includes contacting the body fluid composition with a size exclusion gel having a molecular weight fractionation range or a molecular weight exclusion range such that the size exclusion gel is capable of excluding or fractionating the urine proteins of interest from the remaining proteins in the body fluid composition. The fractionated urine proteins are then quantified by electrophoretic methods, such a capillary zone electrophoresis.

Barden discloses an apparatus for determining the level of sulfuric acid in an atmospheric air sample that contains sulfur dioxide and ammonium sulfates. The apparatus comprises a transport chamber, a collection chamber, a source of dilute hydrochloric acid vapor, a pump means, a source of clean carrier gas, a detector means, and a cyclically operating time clock, and valve means. The measurement of total concentration of sulfuric acid is accomplished using a flame photometric detector (a type of chemiluminescent spectroscopy) which measures total content of sulfur in a sample.

Blatt discloses a method of removing interference from a sample of bodily fluid by contacting the bodily fluid to a filter. The filter has a solid phase support and an active chemical component that binds to the interfering substance. The resulting "clean" bodily fluid sample is analyzed using immunoassays, fluorescing assays, radioimmunoassays, luminescence assays, or assays relying on the quantification of the reflectance or the absorption of a characteristic light wavelength.

A reference cannot anticipate a claimed invention unless it teaches or discloses each element of the claimed invention. In the present case, none of the eight references applied by the Examiner teaches each element of the claimed invention. The invention, as claimed, is a sample solution treating instrument adapted for use with a biosensor that electrochemically measures a specific component in the sample solution, for example, by detection of an oxidation current, wherein the instrument is not physically coupled with such biosensor.

In contrast, at least seven of the references cited by the Examiner as basis for his § 102(b) rejection do *not* teach an instrument adapted for use with a biosensor that accomplishes the analysis by electrochemical measurement. The Yasuda reference teaches use of maleimide to segregate any substances that would interfere with the reaction between the fluorescence inducing reagent and the catecholamine. The sample of Yasuda is then analyzed using a physically attached fluorometer, which detects the fluorescence of the catecholamine fluorophore.

The Rosman applicator is for use in eliminating particulates which may interfere with a subsequently performed immunoassay for detection of various proteins in a sample.

Similarly, the apparatus of Kondo is a filter which removes components and elements of turbidity which would interfere with detection of human chorionic gonadotropin in an immunologic protein assay.

Khanna discloses contacting a serum sample to a chromatographic column to purify the protein of interest (digoxin) which is then quantified using traditional immunologic labeling assays such as enzyme labels, fluorescence assays, or radioimmunoassays.

Liu discloses a gel for separating out urine proteins of a desired size, which are subsequently quantified, based upon their molecular weight, by electrophoretic processes.

Barden discloses elimination of sulfur dioxide and aluminum sulfates in a sample that is subsequently analyzed using a flame photometric detector (a type of chemiluminescence spectroscopy which measures light emission reaction with a combustible gas).

Blatt, similar to Rosman, Kondo, and Khanna, prepares a sample which is then analyzed using traditional labeling assays, such as immuno assays, fluorescing assays, radioimmunoassays, luminescence assays or assays which rely on the measurement of the reflectance and/or the absorption of a characteristic light wavelength. None of the Yasuda, Rosman, Kondo,

Khanna, Lui, Barden, or Blatt references (all discussed above) teaches a control means for converting a sample solution to a condition for analysis by a biosensor which is physically separate from the control means and which electrochemically measures the specific component in the sample solution; therefore, none taken individually teaches each element of the claimed invention.

Additionally, as the applicants have pointed out in their prior response, Barden, in contrast to the invention as presently claimed, teaches a collection chamber (wherein the interfering compounds of sulfur dioxide and ammonium sulfate are segregated from the sulfuric acid) that is unitary with, and therefore physically coupled to, the analytical detector means. *See, e.g.*, Figure 1 of Barden. Similarly, with regard to Bockowski, the filters of Bockowski are located adjacent to the sensor electrode and are contained in close proximity to the sensor in a unitary support housing. Thus, neither Bockowski nor Barden discloses an instrument that is not physically coupled to a sensor, as is presently claimed.

Thus, in view of the foregoing, it is respectfully submitted that none of the references which the Examiner has put forth as anticipatory teaches each element of the invention as claimed. Accordingly, it is respectfully requested that the Examiner reconsider and withdraw each of his rejections under 35 U.S.C. § 102(b) based upon each of Bockowski, Yasuda, Rosman, Kondo, Khanna, Lui, Barden, and Blatt.

CONCLUSION

For the reasons discussed above, it is submitted that the claims are fully compliant with 35 U.S.C. § 112 and patentably distinguishable over all art of record and known to the applicants. Accordingly, reconsideration and allowance of claims 19-28 are earnestly solicited.

Respectfully submitted,

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